
Guidance for Industry

Initial Completeness

Assessments for Type II API

DMFs Under GDUFA

DRAFT GUIDANCE

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For questions regarding this draft document contact Division of Drug Information at 1-866-405-5367.

**U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)**

**October 2012
Generic Drugs**

Guidance for Industry Initial Completeness Assessments for Type II API DMFs Under GDUFA

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TABLE OF CONTENTS

I.	INTRODUCTION.....	1
II.	BACKGROUND	2
III.	INITIAL COMPLETENESS ASSESSMENT	2
A.	Information Confirmed During the Initial Completeness Assessment	3
B.	Check of Initial Completeness Assessment Elements	4
IV.	INITIAL COMPLETENESS ASSESSMENT OUTCOMES	4
V.	API INFORMATION INCLUDED IN A GENERIC DRUG SUBMISSION.....	5
VI.	SUMMARY	5
	DEFINITIONS	6
	APPENDIX 1:.....	7

Guidance for Industry¹
Initial Completeness Assessments for Type II API DMFs
Under GDUFA

This draft guidance, when finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

I. INTRODUCTION

This draft guidance is intended for holders of Type II active pharmaceutical ingredient (API) drug master files (DMFs) that are or will be referenced in an abbreviated new drug application (ANDA) or an amendment or prior approval supplement (PAS) to an ANDA (generic drug submissions). The guidance explains that, beginning October 1, 2012, under the Generic Drug User Fee Amendments of 2012, commonly referred to as GDUFA.²

- DMF holders are required to pay a DMF fee when first authorizing the reference of their DMF in a generic application, and
- Type II API DMFs must undergo an FDA initial completeness assessment.

The guidance makes recommendations about the information that should be included in the DMF to facilitate an initial completeness assessment (CA). The guidance does not apply to new drug applications (NDAs), biologics license applications (BLAs), or other submissions that are not generic drug submissions.³

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

¹ This guidance has been prepared by the Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER) at the Food and Drug Administration (FDA or Agency).

² Public Law 112-144, Title III.

³ See section 744A(7) of Federal Food, Drug and Cosmetic Act (FD&C Act).

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II. BACKGROUND

Under GDUFA, beginning October 1, 2012, the holder of a Type II API DMF must pay a one time DMF fee when it first authorizes in a letter of authorization (LOA) the reference of its DMF in an ANDA, an ANDA amendment, or an ANDA PAS.⁴ Holders of DMFs that were evaluated *before* October 1, 2012 will also be required to pay a fee for the DMF when their DMF is first referenced in a new ANDA, an ANDA amendment, or an ANDA PAS on or after October 1, 2012. The fee amount and fee due date will be announced in a notice in the *Federal Register*. Only Type II API DMFs for use in generic drug submissions incur this one-time fee.

In addition, GDUFA requires Type II API DMFs to undergo an initial CA⁵ to ensure that the DMF is complete. Although the requirement for an initial CA for Type II API DMFs is new, the elements of the initial CA have been used previously by FDA to evaluate DMFs. DMFs that have paid the fee and been found to be complete in accordance with the criteria for an initial CA set out in the attached checklist will be identified on FDA's public Web site as available for reference in support of a generic drug submission. When submitting a DMF, the DMF holder should also submit Form FDA 3794, the Generic Drug User Fee Cover Sheet, which requests the minimum information necessary to determine if a DMF holder has satisfied all relevant user fee obligations.

Note: DMF holders are encouraged, but not required, to submit their DMFs using the Electronic Common Technical Document (eCTD) format. More information is available on the eCTD format on FDA's Web site and in the ICH guidance M4Q.⁶

III. INITIAL COMPLETENESS ASSESSMENT

FDA will perform an initial CA once a DMF holder files a Type II API DMF⁷ with the generic drug user fee cover sheet (Form FDA 3794) and the fee payment has been verified. *Note:* the initial CA does not replace the full scientific review, which is performed to determine the adequacy or inadequacy of the information contained in the DMF to support an ANDA review decision.

In brief, FDA will undertake an initial CA to determine the following:

- Is the DMF active?
- Has the fee been paid?

⁴ Section 744B(a)(2) of the FD&C Act. For discussion of letters of authorization, see 21 CFR 314.420(b) and 314.50(g)(1).

⁵ Section 744B(a)(2)(D)(ii) of the FD&C Act.

⁶ See information about electronic submissions at:

<http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/ucm153574.htm> and ICH M4Q:

http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/CTD/M4_R1_Quality/M4Q_R1_.pdf.

⁷ See Drug Master Files at:

<http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFiles/default.htm>.

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- Has the DMF been previously reviewed?
- Does the DMF pertain to a single drug substance?
- Does the DMF contain certain administrative information?
- Does the DMF contain all the information necessary to enable a scientific review?⁸
- Is the DMF written in the English language?⁹

FDA will conduct the initial CA by completing a series of questions listed in the GDUFA Initial Completeness Assessment Checklist for Type II API DMFs, which is included in Appendix 1. This guidance provides additional detail on the kinds of information FDA will confirm when performing an initial CA on a DMF.

A. Information Confirmed During the Initial Completeness Assessment

FDA will use the initial CA Checklist (see Appendix 1) to perform the initial CA. At the top of the cover page of the checklist, FDA will fill in basic information about the DMF, including its name, number, receipt date, and whether the DMF was submitted in electronic or paper format. The FDA will also note whether the primary DMF that is referenced by the ANDA contains any references to other DMFs (subject DMFs). A primary DMF can reference subject DMFs (such as a DMF that describes the manufacture of a material used in producing the active ingredient),¹⁰ which provides additional information needed to completely describe the manufacture of a drug substance.

Note: Before submitting its DMF, the primary DMF holder should check with the holders of any referenced subject DMFs to make sure that they are filed with FDA and are still considered active DMFs. If a referenced DMF is not yet filed or has become inactive, FDA would consider the primary DMF to be incomplete.

1. Confirm that DMF fee has been paid.

Before assigning a DMF to a reviewer for an initial CA, FDA will confirm that the DMF fee has been paid. If the fee has not been paid, FDA will not assign the DMF to a reviewer for an initial CA. *Note:* ANDA applicants that reference a DMF for which a fee is due but has not been paid will be notified that the DMF holder has not paid the fee. If the DMF fee is not paid within 20 days after notification, the ANDA referencing the DMF will not be received.

2. Is the DMF active?

If the primary DMF or any referenced subject DMFs on file at FDA are inactive, FDA will consider the primary DMF incomplete and send the DMF holder a letter notifying them that the DMF is incomplete and identifying the missing elements in the DMF that must be addressed.

⁸ See Drug Master Files at:

<http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/default.htm>, and

ICH M4Q: http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/CTD/M4_R1_Quality/M4Q_R1.pdf.

⁹ If a DMF contains information in another language, an accurate certified English translation must also be included.

¹⁰ If a subject DMF does not meet the definition of a Type II API DMF, it will not incur a DMF fee.

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3. Has the DMF been previously reviewed for chemistry, manufacturing, and controls (CMC) by FDA in the context of a review of a prior application?

If FDA has reviewed the DMF for CMC after November 30, 2007, the DMF will be considered to have passed the initial CA without further analysis. If the DMF has not previously received this full review, then it will be assigned to a reviewer for an initial CA.

B. Check of Initial Completeness Assessment Elements

FDA also will complete the administrative part of the checklist (General Information) during the initial CA. The DMF will be deemed incomplete if any item in the checklist is marked “no” (other than item #2, which asks if the DMF needs to be updated and an answer of “yes” will result in an incomplete status). Then, FDA will send the DMF holder an Incomplete Letter. Generally, this letter will provide comments about each element that resulted in an incomplete designation for the initial CA. Exceptions are specified in this guidance document.

If an item is marked “n/a,” and the element does not apply to the DMF, then element is treated the same as if it were marked “yes.”

1. Subject of the DMF is a single drug substance produced by one manufacturing process

A DMF should be limited to one drug substance and one manufacturing process. If a DMF includes information for more than one drug substance, or if it contains more than one manufacturing process, the DMF will be deemed incomplete. If the DMF describes multiple drug substances, the DMF holder should file separate DMFs for each substance. Similarly, if there are multiple manufacturing processes for a drug substance, the DMF holder should file separate DMFs for each manufacturing process.

2. DMF holder needs to submit a complete update

If it has been 5 years or more since the DMF has received a complete update, or if there have been more than a combination of 5 amendments and annual updates to the DMF, the DMF holder should provide a complete and comprehensive update to it. If the DMF does not include such an update, FDA will consider the DMF incomplete.

FDA believes that the remainder of the initial CA checklist is self-explanatory.

IV. INITIAL COMPLETENESS ASSESSMENT OUTCOMES

Following the initial CA, FDA will find the DMF either complete or incomplete. If the DMF is found complete, FDA will post the DMF number on a publicly available list on FDA’s Web site to indicate that the DMF is available for reference by generic drug applicants.¹¹

¹¹ For the public list of DMFs available for reference, see www.fda.gov/gdufa.

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If the DMF is incomplete, the initial CA findings and comments will be compiled in an Incomplete Letter to the DMF holder explaining why the DMF was found incomplete. Information about the initial CA status of a DMF, other than public listing on the Web site, will not be provided to anyone except for the DMF holder.

V. API INFORMATION INCLUDED IN A GENERIC DRUG SUBMISSION

If a generic drug submission contains all the necessary API information and does not rely on information contained in a DMF, no initial CA will be needed. However, because GDUFA requires collection of a one-time fee for API information included in a generic drug submission (i.e., an (a)(3)(F) fee),¹² the applicant submitting the generic drug submission containing the API information will be required to pay this fee.

VI. SUMMARY

In summary, once the DMF fee is received, FDA will evaluate the DMF to make sure it meets the initial CA criteria.

- If the DMF passes the initial CA, the DMF number will be made publicly available on FDA's Web site.
- If the DMF fails the initial CA, FDA will send an Incomplete Letter describing the missing elements to the DMF holder.
- If a generic drug submission contains all the necessary API information and does not reference a DMF, the applicant will be required to pay the (a)(3)(F) fee. No initial CA will be conducted.

¹² Section 744B(a)(3)(F) of FD&C Act.

DEFINITIONS

Active Pharmaceutical Ingredient¹³ (as defined by GDUFA):

- (A) a substance, or a mixture when the substance is unstable or cannot be transported on its own, intended—
 - (i) to be used as a component of a drug; and
 - (ii) to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease, or to affect the structure or any function of the human body; or
- (B) a substance intended for final crystallization, purification, or salt formation, or any combination of those activities, to become a substance or mixture described in subparagraph (A).

Active DMF: A DMF for which FDA has made a determination that the DMF was acceptable for filing administratively, and is up-to-date.

DMF Holder¹⁴: Designated owner of the DMF, which may be different from the U.S. agent listed as the contact.

Generic Drug Submission¹⁵: An abbreviated new drug application (ANDA), an amendment to an ANDA, or a prior approval supplement (PAS) to an ANDA.

Letter of Authorization (LOA)¹⁶: A written statement by the holder or designated US agent or representative permitting FDA to refer to information in the DMF in support of another person's generic drug submission.

Type II Active Pharmaceutical Ingredient Drug Master Files¹⁷: Information submitted by a person that intends to authorize FDA to reference the information to support approval of a generic drug submission without the submitter having to disclose the information to the generic drug submission applicant. In addition, the submission provides confidential detailed information about facilities, processes, or articles used in the manufacturing, processing, packaging, and storing of the drug substance (or drug substance intermediate and material used in preparation of drug product).

¹³ Section 744A(2) of FD&C Act.

¹⁴ See 21 CFR 314.420(a).

¹⁵ Section 744A(7) of FD&C Act.

¹⁶ See Drug Master Files at:

<http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/default.htm>.

¹⁷ Section 744A(12) of FD&C Act; also see 21 CFR 314.420(a)(2).

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**APPENDIX 1: GDUFA INITIAL COMPLETENESS ASSESSMENT CHECKLIST FOR
TYPE II API DMFs**

DMF: (NAME/ NUMBER)

HOLDER:

DRUG NAME (Subject):

LETTER DATE:

RECEIVED DATE:

Electronic or Paper Submission:

DMF(s) referenced by the primary DMF being assessed, if applicable:

☐ EXPEDITED ASSESSMENT per REQUEST from FDA by: (requestor name here)

Primary Reviewer:

Date:

Review Recommendation for Initial Completeness
Assessment:

☐ COMPLETE ☐ INCOMPLETE

1. Has the GDUFA fee been paid? Enter date paid:

☐ Yes ☐ No

2. Is the DMF active?

☐ Yes ☐ No

If no, DMF is INCOMPLETE per policy. Issue Incomplete Letter to DMF holder.

3. Has the DMF been reviewed, after November 30, 2007, for chemistry, manufacturing and controls (CMC) by
FDA in the context of a review of a prior application?

☐ Yes ☐ No

If “yes,” the DMF is COMPLETE per policy.

If “no,” review DMF with checklist.

ADDITIONAL COMMENTS REGARDING THE DMF:

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Checklist Review

GENERAL INFORMATION

			NOTE(S)
	<p>1. Subject of the DMF is a single drug substance produced by one manufacturing process.</p> <p>2. For previously submitted DMFs, the DMF holder needs to submit a complete update.</p> <p>3. cGMP Statement of Commitment is provided.</p> <p>4. Complete name, address, and contact information for holder and all manufacturing and testing facilities provided.</p> <p>5. U.S. Agent designated for non-U.S. DMF holders with appropriate designation letter.</p> <p>6. Contains Letters of Authorization for any DMFs referenced to support this DMF.</p> <p>7. All DMFs referenced by this DMF have been filed with the Agency and are active.</p> <p>8. Contains label with storage conditions and expiry/retest date.</p> <p>9. Contains BSE/TSE certification if animal sourced.</p> <p>10. Contains information on adventitious agents if animal sourced.</p> <p>11. Contains information on presence of pesticides if plant sourced.</p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> n/a</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> n/a</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> n/a</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> n/a</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> n/a</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> n/a</p>	<p>For #1, if the DMF contains information concerning more than a single drug substance, or more than a single manufacturing process, the DMF will be considered incomplete and the firm will be asked to amend the DMF to a single substance and/or process as the case may be. The assessment will continue when the updated information is provided.</p> <p>For #2, the necessity for submission of the update is due to the large number of amendments and updates and/or length of time since the original submission or last complete update. If the DMF needs to be updated, it will be considered incomplete. The initial completeness assessment will continue when the updated information is provided. This is the only item for which the answer of “yes” would result in the DMF being incomplete.</p> <p>BSE: Bovine Spongiform Encephalopathy TSE: Transmissible Spongiform Encephalopathy</p>

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274 **MODULE 2: SUMMARIES¹**

eCTD No.			NOTE(S)
2.3	12. Contains a <u>Quality Overall Summary</u> (QoS).	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> n/a	

275 276 277 **MODULE 3: QUALITY**

278 **3.2 Body of Data**

279 **3.2.S DRUG SUBSTANCE [name, manufacturer]**

eCTD No.			NOTE(S)
3.2.S.1	General Information Contains complete <u>General Information</u> on the following: 13. Nomenclature 14. Structure 15. General Properties: Should contain basic information regarding the general properties of the drug substance.	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Yes <input type="checkbox"/> No	
3.2.S.2	Manufacture 3.2.S.2.1 Contains complete <u>Manufacturer Information</u> on the following for each site: 16. Name and Full Address(es) of the Manufacturing Facility(ies) Contact name of on-site individual, phone and fax numbers, email address	<input type="checkbox"/> Yes <input type="checkbox"/> No	<p>Note: If a late stage intermediate has been outsourced, detailed information regarding the source for each supplier needs to be provided in section 2.3.</p> <p>Separate facilities used for release testing of the API and for additional processing (e.g. micronization) should also be listed.</p> <p>Central File Number or Facility Establishment Identifier numbers should be provided if available.</p>

¹ DMF holders are encouraged, but not required, to submit files in eCTD format. See information about electronic submissions at:

<http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/ucm153574.htm> and ICH M4Q:

http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/CTD/M4_R1_Quality/M4Q_R1_.pdf.

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eCTD No.			NOTE(S)
	<p>3.2.S.2.2 Contains <u>Description of Manufacturing Process and Process Controls</u> addressing the following:</p> <p>17. If API is synthetic, complete Synthetic Scheme from <u>appropriately supported starting materials</u>. Scheme includes structural representation with reagents, reaction conditions, etc.</p> <p>18. Flow chart for every stage.</p> <p>19. Description of the manufacturing process.</p> <p>3.2.S.2.3 Contains information on the <u>Control of Materials</u>, as follows:</p> <p><i>Starting Material:</i></p> <p>20. Name of each supplier</p> <p>21. Specification</p> <p>22. Analytical protocol</p> <p>23. Certificate of Analysis (CoA) from supplier.</p> <p>24. CoAs from the DMF Holder</p> <p><i>Reagents/Solvents:</i></p> <p>25. Specifications</p> <p>26. Test Methods</p> <p>27. Representative CoAs</p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> n/a</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No</p>	<p>Note: DMF will not be considered complete for review requirements if the <u>complete process</u> is not included in the DMF or by appropriate reference to another DMF. If the firm chooses intermediates as “starting materials” a determination should be made if information is provided in the DMF to adequately evaluate their controls and effect on the drug substance quality and purity.</p> <p>Note: Specification, analytical protocol and representative CoA of each reagent/solvent should be provided.</p>

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eCTD No.			NOTE(S)
	<p>3.2.S.2.4 Contains information for <u>Controls of Critical Steps and Intermediates</u> as follows:</p> <p>28. In-process controls:</p> <p>29. Critical steps are identified.</p> <p>30. Controls are described for each critical step.</p> <p><i>Intermediates:</i></p> <p>31. Isolated intermediates are identified.</p> <p>32. Specifications for each identified intermediate.</p> <p>33. Analytical methods provided for each intermediate.</p> <p>3.2.S.2.5 Process Validation and/or Evaluation</p> <p>34. Contains a summary of <u>Process Validation and/or Evaluation</u> information.</p> <p>35. Sterility assurance data is provided.</p> <p>3.2.S.2.6 Manufacturing Process Development</p> <p>36. Contains a summary of <u>Manufacturing Process Development</u>.</p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> n/a</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> n/a</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No</p>	<p>For sterile APIs.</p>

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eCTD No.			NOTE(S)
3.2.S.3	<p>Characterization</p> <p>3.2.S.3.1 Information is provided to support the <u>Elucidation of Structure and other Characteristics of the Drug Substance</u> as follows:</p> <p>37. Basic characterization information appropriate for the material (i.e., NMR, IR, UV, MS, Elemental Analysis etc.).</p> <p>3.2.S.3.2 Information is provided on <u>Impurities</u> as follows:</p> <p>38. A table including the name(s), structure(s), origin (degradant, process impurity) of observed/potential organic impurities is provided.</p> <p>39. Information is provided on potential <u>Impurities (inorganic)</u> (i.e., metal catalysts, reagents etc.)</p> <p>40. Information is provided on potential <u>residual solvents</u> consistent with USP <467>.</p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No</p>	
3.2.S.4	<p>3.2.S.4 Information is provided to support the <u>Control of the Drug Substance</u> as follows:</p> <p>41. Full test specification is provided.</p> <p>42. Description of the analytical methods is provided.</p> <p>43. Method Validation and/or method verification reports are provided.</p> <p>44. Certificates of Analysis for</p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No</p>	<p>Method validation reports may be included in section 3.2.R.3.S.</p>

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eCTD No.			NOTE(S)
	<p>representative batches are provided (batch analysis).</p> <p>45. Justification for each specification is provided.</p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No</p>	
3.2.S.5	<p>Information is provided to support the <u>Reference Standards or Materials</u> as follows:</p> <p><i>Drug substance:</i></p> <p>46. The source, Lot#, CoA (for primary Reference Standard (RS) and Working Standard (WS)) are provided.</p> <p>47. Physical/chemical characterization data for non-USP reference standards are provided.</p> <p>48. For a compendial drug substance, comparative data between the USP RS and the in-house WS are provided.</p> <p><i>Impurities:</i></p> <p>49. The source, Lot#, CoA for RS and WS are provided for each identified impurity.</p> <p>50. Physical/chemical characterization data for non-USP reference standards are provided.</p> <p>51. For impurities with</p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> n/a</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> n/a</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> n/a</p>	

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eCTD No.			NOTE(S)
	compendial RS available, comparative data between the USP RS and the in-house WS is provided.	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> n/a	
3.2.S.6	<p>Information is provided to support the <u>Container Closure System</u> as follows:</p> <p>52. Description of container closure system is provided (including contact material and secondary material).</p> <p>53. Certification statements for contact materials for use in food and drugs are provided.</p> <p>54. Source, specifications and Representative CoA for each material is provided.</p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No</p>	
3.2.S.7	<p>Information is provided to support the <u>Stability</u> of the drug substance as follows:</p> <p>3.2.S.7.1 Stability Summary and Conclusions</p> <p>55. Retest date or expiration date of drug substance is clearly indicated.</p> <p>3.2.S.7.2 Post-approval Stability Protocol and Stability Commitment</p> <p>56. Stability protocol is provided.</p> <p>57. Stability commitment is provided.</p> <p>3.2.S.7.3 Stability Data</p> <p>58. Stability Data is provided.</p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No</p>	

280
281

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282

283

MODULE 3: 3.2.R REGIONAL INFORMATION (Drug Substance)

			NOTE(S)
3.2.R	<p>Regional information is provided as follow:</p> <p>3.2.R.1.S Executed Batch Records for drug substance</p> <p>59. Firm includes representative Executed Batch Records with translation, where appropriate.</p> <p>60. Yields, results of in-process controls, and analytical results for intermediates are provided.</p> <p>3.2.R.2.S Comparability Protocols</p> <p>61. Comparability protocols are provided if applicable.</p> <p>3.2.R.3.S Methods Validation Package</p> <p>62. Methods Validation Package is provided.</p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> n/a</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No</p>	<p>Method validation package may be included in section 3.2.S.4.</p>

284